

Claims

1           1.     A method for treating a subject suffering from cancer, said  
2 method comprising the step of:

3                 administering to a subject a therapeutically effective amount of a herpes  
4 simplex virus (HSV) comprising a nucleic acid sequence encoding for an agent  
5 selected from the group consisting of interleukin-12, granulocyte macrophage  
6 colony stimulating factor, and cytosine deaminase such that an anti-cancer  
7 response is induced in the subject.

1           2.     A method according to claim 1, wherein said administering step  
2 comprises intratumorally disposing the HSV into the subject.

1           3.     A method according to claim 1, wherein the HSV vector is  
2 substantially aneurovirulent.

1           4.     A method according to claim 3, wherein the HSV vector is  
2 replication competent.

1           5.     A method according to claim 3, wherein the HSV vector  
2 comprises a deletion of the  $\gamma_134.5$  gene.

1           6.     A method according to claim 5, wherein IL-12 genes are  
2 inserted within the  $\gamma_134.5$  gene deletion.

1           7.     A method according to claim 6, wherein the IL-12 genes  
2     comprise subunits p35 and p40 separated by an IRES sequence.

1           8.     A method according to claim 7, wherein said IL-12 encoding  
2     nucleic acid sequence bicistronically expresses the p35 and p40 subunits to  
3     produce self-assembling, heterodimeric IL-12 in the HSV vector.

1           9.     An anti-tumor pharmaceutical composition comprising a herpes  
2     simplex virus (HSV) vector comprising a nucleic acid sequence encoding for a  
3     compound selected from the group consisting of IL-12, GM-CSF, and CD  
4     operatively linked to a promoter, and a pharmaceutically acceptable carrier.

1           10.    A pharmaceutical composition according to claim 9, wherein  
2     said HSV vector is substantially aneurovirulent.

1           11.    A pharmaceutical composition according to claim 9, wherein  
2     said HSV vector is replication competent.

1           12.    A pharmaceutical composition according to claim 9, wherein  
2     said HSV vector has been transformed with an expression cassette comprising  
3     nucleic acid sequences encoding for the p40 and p35 of IL-12, said subunits  
4     being separated from each other by an IRES encoding sequence.

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1           13.    A pharmaceutical composition according to claim 12, wherein  
2    said HSV vector includes a deletion of the  $\gamma_134.5$  gene.

1           14.    A pharmaceutical composition according to claim 9, wherein the  
2    expression of the nucleic acid sequence encoding for IL-12 results in  
3    constitutive production of IL-12 in vivo.

1           15.    A pharmaceutical composition according to claim 9 which has  
2    been formulated for injection.

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